Alberta Heritage Foundation
for Medical Research

Interventional and Intraoperative Magnetic Resonance Imaging

Executive Summary

Background

MRI technology uses a magnetic field to non-invasively produce cross sectional images, based on the distribution of water and lipids within tissues, of structures inside the body. The limitations of conventional interventional/intraoperative imaging techniques, such as fluoroscopy, computed tomography, ultrasound, and stereotactic navigation, have led to the development of interventional/intraoperative MRI in an attempt to optimise lesion localisation and surgical planning. The purported advantages of interventional/ intraoperative MRI over other imaging methods include excellent soft tissue contrast; increased surgical precision and resection control; a lower likelihood of reoperation; and the ability to visualise tissue changes, such as brain shift, and acute complications in real-time as surgery proceeds.

Objectives

To provide an overview of the use of real-time magnetic resonance imaging (MRI) during interventional and surgical procedures with respect to safety, efficacy/effectiveness, cost, and utilisation within Canada. The report will be used to assist Capital Health in future planning decisions on interventional/intraoperative MRI capacity within the health region.

Results

Only four non-randomised comparative studies met the inclusion criteria: one on interventional MRI and three on intraoperative MRI. Patients who underwent interventional MRI guided brain biopsy had similar postoperative morbidity rates to those who underwent a stereotactic technique. However, one fatality occurred following conventional stereotactic biopsy, whereas no deaths occurred in the interventional MRI group.

Using intraoperative MRI to monitor brain tumour resection resulted in a substantial increase in operative time, compared to conventional surgery, but with no discernible effect on the perioperative anesthetic outcome of patients. Conversely, the hospital stay was generally shorter after the intraoperative MRI procedure. The use of intraoperative MRI for resection control of supratentorial cavernous hemangiomas made no difference to the amount of pathology resected, compared to standard neuronavigation techniques, whereas significantly more tumour volume was resected in patients with high grade gliomas. None of the included studies reported any adverse events directly related to the use of intraoperative MRI, but this was also true for the conventional procedures that intraoperative MRI was compared to.

The results may underestimate the capabilities of interventional/intraoperative MRI because of substantial confounding from the learning curve effect, but the presence of methodological flaws

in the studies made it impossible to characterise the overall magnitude or direction of these biases. Thus, it is unclear whether the equivocal results are a consequence of limitations in study design, the interventional/intraoperative MRI procedure itself, or both. The included studies only used MRI as a tool to guide or monitor interventional and operative neurosurgical procedures. Therefore, the clinical utility of using MRI to guide or monitor any other type of intervention or surgery, such as percutaneous biopsy or endoscopic abdominal surgery, is unknown.

There are currently four interventional/intraoperative MRI facilities in Canada, which are located in Calgary, Winnipeg, Quebec City, and Toronto. Two other centres in Halifax and Ottawa may acquire an interventional/intraoperative MRI unit in the near future.

Conclusions and Recommendations

Interventional and intraoperative MRI is a high cost, developmental technology for which no major safety concerns have been identified to date. Due to its recent genesis, the scope, applicability, efficacy, and cost effectiveness of this technology have not been established. Concurrently controlled studies assessing the impact of interventional/intraoperative MRI on patient management and outcomes will provide the information required to resolve the question of whether interventional/intraoperative MRI has a broader clinical application beyond its current use in the research setting. As more interventional/intraoperative MRI systems are installed, such trials may become feasible.

Methodology

All original, published randomised controlled trials and non-randomised comparative studies, with at least ten patients in each study arm, were identified by systematically searching PubMed, EMBASE, HealthStar, The Cochrane Library, Science Citation Index, and the web sites of various health technology assessment agencies, research registers, and guidelines sites from January 1990 to January 2004. No language restriction was applied. Only studies of interventional or surgical procedures that utilised near real-time MRI to guide or monitor aspects of the procedure at the time that it was being performed were included.

Reference:

Scott A. *Interventional and intraoperative magnetic resonance imaging.* Edmonton, AB: Alberta Heritage Foundation for Medical Research; March 2004 (IP 18).

The full text is available at http://www.ahfmr.ab.ca/programs.html

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105-01956/

Alberta Heritage Foundation
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Interventional and Intraoperative Magnetic Resonance Imaging

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March 2004

IP 17: Information Paper

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This Information Paper has been prepared on the basis of available information of which the Foundation is aware from public literature and expert opinion, and attempts to be current to the date of publication. It has been externally reviewed. Additional information and comments related to the report are welcome and should be sent to:

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ISBN 1-896956-92-0 (Print)
ISBN 1-896956-94-7 (On-Line)

ISSN: 1706-7863

Alberta's Health Technology Assessment program has been established under the Health Research Collaboration Agreement between the Alberta Heritage Foundation for Medical Research and the Alberta Health Ministry.

ACKNOWLEDGEMENTS

The Alberta Heritage Foundation for Medical Research is grateful to the following persons for provision of information and for comments on the draft report.

Dr. Keith Aronyk, Chief of Pediatric Surgery, Stollery Children's Hospital, Edmonton, Alberta

Dr. Robert Brownstone, Division of Neurosurgery, Dalhousie University, Halifax, Nova Scotia

Dr. Walter Kucharczyk, Professor and Chair, Department of Medical Imaging, Faculty of Medicine, University of Toronto, Toronto, Ontario

Dr. Garnette Sutherland, Professor, Department of Clinical Neurosciences, Faculty of Medicine, University of Calgary, Calgary, Alberta

Information Services Support

Ms. Seana Collins, Research Librarian, Alberta Heritage Foundation for Medical Research, Edmonton, Alberta

Ms. Sandra Shores, Health Sciences Librarian, John W. Scott Health Sciences Library, University of Alberta, Edmonton, Alberta.

The views expressed in the final report are those of the Foundation.

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SCOPE OF THE PAPER

This response addressed a request from the Capital Health regional authority in Alberta. The objective of this Information Paper is to provide an overview of the use of real-time magnetic resonance imaging during interventional and surgical procedures with respect to safety, efficacy/effectiveness, cost, and utilisation within Canada. The report is intended to assist Capital Health in future planning decisions on interventional/intraoperative magnetic resonance imaging capacity within the health region.

BACKGROUND

Magnetic resonance imaging technology

In principle

Magnetic resonance (MR) imaging technology utilises the principle of nuclear MR to non-invasively view structures inside the human body. Nuclear MR was first discovered in 1946. However, the principle was not applied to imaging until 1973, with the first (nuclear) MR scanner becoming available in 1977 [1,2].

A proton within the nucleus of an atom possesses charge, mass, and angular momentum or spin. Thus, a proton gyrates or precesses about its axis in the same way that a spinning top wobbles. This motion generates a magnetic field that makes the proton behave like a tiny bar magnet with a north and south pole oriented along the spin axis. When protons are placed in a much stronger magnetic field, they align themselves either parallel or antiparallel to the direction of the external magnetic field. In this environment, the application of a radio wave (radiofrequency radiation) can cause some of the protons to absorb energy and momentarily shift out of alignment with the magnetic field or resonate. The wavelength of radiofrequency energy absorbed is unique to the type of atom and its chemical environment, a characteristic referred to as chemical shift. When the radiofrequency pulse is turned off, the protons return to their natural alignment with the external magnetic field and release the excess stored energy as a weak radio signal of the same frequency as the original radio wave [1-3].

MR imaging can only be applied to magnetic nuclei, which typically have unpaired protons or neutrons, or both. Potassium (^{31}K), carbon (^{13}C), and phosphorus (^{31}P) have been used in MR imaging studies, but hydrogen (^{1}H), fluorine (^{19}F), and sodium (^{23}Na) give the best image resolution. Useful MR images of the human body can only be obtained if the nuclei targeted are ubiquitous in biological tissues. Consequently, MR imaging is usually directed at hydrogen nuclei (also known as proton MR imaging) since they comprise nearly two thirds of the atoms in the human body. The resultant images are based on the distribution of water and lipids within the tissues [2-4].

In practice

In an MR scan examination, the patient is placed in the bore of a large magnet until the body part being scanned is in the exact centre or isocentre of the magnetic field. A radiofrequency coil or antenna is placed over the body part to induce the aligned hydrogen nuclei in the patient's tissues to resonate. Within milliseconds, the atoms relax back into their pre-resonant state and emit a weak radio signal that is picked up by the radiofrequency coil. Gradient magnets arranged inside the main magnet create a

magnetic field whose strength varies in a linear direction. These magnets alter the main fixed magnetic field in precise planes or slices across the body to create resonant conditions only for those protons located in that predetermined slice. Thus, the exact spatial position of the resonating hydrogen atoms can be pinpointed, which enables multiplanar imaging without having to move the patient. These data are then relayed to a computer and processed by complex algorithms to create a cross-sectional image of the body [2,5,6].

Three dimensional images are produced by assembling a series of consecutive two dimensional images one on top of the other. The final MR image is based on a complex set of tissue parameters including hydrogen density, motion, flow, chemical shift, and relaxation time. In diagnostic scanning, a typical examination comprises a series of two to six scan sequences, each of which lasts from 2 to 15 minutes. A typical MR examination can last from 10 to 60 minutes, depending on the type of imaging required [2,5-7].

MR imaging hardware

There are three basic types of magnets used in MR imaging: permanent, resistive, and superconducting. Permanent magnets are constructed from permanently magnetised material and are relatively inexpensive to install, operate, and maintain. However, these magnets are sensitive to changes in temperature and are extremely heavy, which limits them to relatively low field strengths. Resistive magnets consist of many coils of wire wrapped around a bore. An electric current is passed through the wire to generate a magnetic field. These magnets are less costly to produce than superconducting magnets and, unlike permanent magnets, the magnetic field can be extinguished by disconnecting the electricity supply. The down side is that very large currents (100 to 150 amperes) are required to generate a magnetic field, which makes the cost of powering and cooling magnets with field strengths above 0.3 tesla (T) prohibitive. Superconducting magnets are the most commonly used in MR scanners. The design is similar to that of a resistive magnet except that the coiled wire is supercooled by submersion in liquid helium to eliminate its inherent electrical resistance. This reduces power consumption and makes the magnet more economical to run. Superconducting magnets can easily generate fields ranging from 0.5 to over 2.0 T [2,8].

MR scanners are available in field strengths that range from 0.02 to 3.0 T. Diagnostic MR scanners generally have a field strength of 1.5 T (15,000 gauss), which is 30,000 times stronger than the earth's magnetic field. Interventional or intraoperative MR scanners range in strength from 0.2 to 1.5 T, with gradient coils generating fields of 18 to 27 mT. Magnets are often described as having a low (0.035 to 0.3 T), mid (0.5 to 1.0 T) or high field (≥ 1.5 T) strength. The field strength of a magnet decreases exponentially with increasing distance from its bore. However, this fringe field can still exert a strong

magnetic pull so lines indicating the 0.5 mT and 5 mT (5 and 50 gauss) perimeter of the magnetic field are usually marked on the floor surrounding an MR scanner [6, 8-10].

Conventional imaging techniques for interventional and surgical procedures

Fluoroscopy and computed tomography

Fluoroscopy became widely available in 1979 and is now one of the most common intraoperative imaging modalities, being widely used in orthopedic surgery, neurosurgery, and interventional cardiology [11, 12]. It uses X-rays to project a real-time two dimensional image onto a fluorescent screen in order to guide instruments or determine the configuration of various anatomical structures. Fluoroscopy is relatively easy to use but is mainly of value for identifying bony landmarks [11-13].

Computed tomography (CT), which was introduced in the early 1970s, adds a third dimension to X-ray images. A beam of X-rays is rotated 360° in a spiral motion around the body part being scanned as the patient passes through the CT scanner. A computer varies the X-ray intensity according to the type of tissue being scanned and then compiles the multiple projections into a cross-sectional image of the body. Intraoperative CT has been used during neurosurgical procedures for over two decades, and has been increasingly used in other areas such as orthopedic and abdominal surgery [12, 14]. Image acquisition is relatively fast, with scanning times of between 5 and 15 minutes, and three dimensional image reconstructions can be obtained. A scan can be performed intraoperatively without removing surgical instrumentation or equipment, or reducing access to the patient [11, 15, 16]. The major drawback of CT is that it uses hazardous ionising radiation. A CT of the abdomen exposes the patient to a dose of radiation that is equivalent to over 300 chest X-rays [17]. CT provides particularly good images of bone, but has poor soft tissue contrast [14, 16].

Stereotactic methods

Neurosurgeons have been at the forefront of developments in image guided surgery in an attempt to optimise lesion localisation and surgical planning [12]. The first stereotactic apparatus clinically deployed to guide neurosurgery was constructed in the late nineteenth century, but this method has only really come to the fore in the latter half of the twentieth century as a result of the parallel advances that occurred in computing and volumetric imaging. Stereotactic navigation systems have now become an integral part of many routine neurosurgical procedures [18, 19].

Frame-based navigation systems use a rigid stereotactic frame that is screwed to the patient's head prior to the operation to generate a three dimensional map of the surgical site based on preoperative CT or MR images. Patients are then operated on with the frame in situ to ensure accurate navigation of instruments to the surgical target [14, 20, 21]. Frameless systems use either anatomical landmarks or a set of fixed external markers

attached to the scalp with adhesive as fiducials, in lieu of a frame, to establish the coordinates of the surgical site [9, 14, 22]. Localisation of surgical instruments and probes is achieved with a variety of methods including optical, magnetic, and ultrasound digitisers or articulated robotic arms [20, 23]. However, since frame-based navigation systems cannot be used during conventional surgical operations, such as craniotomy, their application is limited to a relatively small subset of procedures [24].

Stereotactic navigation has increased the accuracy of lesion localisation and reduced the invasiveness of many neurological procedures [25, 26]. The precision of stereotactic navigation systems depends on a number of factors including the preoperative image quality; the inherent technical accuracy of the system; the accuracy of the registration process, which projects the three dimensional preoperative images onto the corresponding anatomy of the patient; and the maintenance of consistent alignment between the coordinate systems, in both real and virtual space, and the patient's head [14, 22, 27, 28].

The biggest contributor to inaccuracy in stereotactic navigation systems is positional shifting, which can be either external, such as when the head moves relative to the reference arc, or internal, due to movement of brain tissues [20, 22]. The latter post-imaging brain deformation, commonly referred to as brain shift, is due to the combined effects of direct physical and indirect physiological manipulation of the brain. These stressors include the loss of cerebrospinal fluid; the impact of gravity, retraction, and tissue resection; the accumulation of air in the subdural or intraventricular spaces; and edema. The use of osmodiuretic agents and hyperventilation to reduce intra-cranial pressure, plus the metabolism lowering effects of anesthetics, also contribute to brain shift [14, 22, 29, 30].

Brain shift is generally a slow process. However, since the neuronavigation system relies on preoperative images for brain mapping, significant inaccuracies can manifest by the end of a lengthy operation [22, 29]. For example, brain surface shifts of over 10 mm have been observed in some patients an hour after opening the dura mater but before tumour resection [31], while sub-surface shifts can be as large as 7 mm at the level of the ventricles [30]. This problem is exacerbated in patients with hydrocephalus, which is often associated with pineal region mass lesions, or in patients who have pre-existing brain shrinkage, such as the elderly [32, 33].

Thus, the lack of real-time imaging during a neurosurgical procedure means that the operative approach may not be optimal, particularly in the current era of small cranial openings and confined surgical corridors. The instruments are not tracked in real-time as they pass through intervening normal tissue, and any alteration in the position of internal tissues cannot be compensated for in the surgical approach [29, 34]. In addition, surgical complications, such as edema or hemorrhage, may not be detected until the

patient awakens from anesthesia, which necessitates in-hospital observation and postoperative imaging [29, 34].

Ultrasound

Intraoperative ultrasound has been used in neurosurgery for nearly twenty years. This technology uses the deflection of sound waves by tissue to construct images of internal structures. High end ultrasound devices can provide real-time visualisation of both anatomy and blood flow [16]. The ultrasound probe must be directly applied to the surgical site, which makes the scans inherently stereotactic because the frame of reference is the transducer itself. Orientation has been further improved recently with the successful integration of three dimensional ultrasound images into neuronavigation systems, thereby enabling intraoperative image updates for visualising brain shift [16, 35]. Ultrasound is relatively inexpensive, compared to other imaging modalities, and does not require the use of special compatible surgical instruments. It is capable of tracking advancing surgical instruments, offers fast multiplanar imaging, and is particularly useful in defining fluid filled spaces, such as cystic lesions [11, 14, 35, 36].

However, ultrasound waves cannot penetrate air or bone. Consequently, ultrasound cannot be used for preoperative imaging of the brain, and the intraoperative view is restricted by the size and position of the craniotomy [12, 16]. It also has limited resolution and spatial definition such that lesions smaller than 5 mm or deeper than 5 cm are difficult to visualise [14, 16, 20]. Improving resolution by using higher sound wave frequencies is counterproductive since lower frequency waves have a greater depth of penetration [12, 16]. The quality of ultrasound images is severely compromised by air bubbles, calcifications, and implanted material, such as brachytherapy seeds. Blood accumulation is difficult to discern on ultrasound scans, as are tumour margins, particularly those of low grade gliomas or tumours whose edges are covered by blood clots [16, 35]. However, contrast agents are currently being developed that may make extravascular blood more visible [35]. As with diagnostic ultrasound, the technique is highly operator dependent and requires a skilled radiology technician to assist in image interpretation [11].

Interventional and intraoperative MR imaging

Development

The multiplanar imaging capability, high spatial and contrast resolution, and capacity for providing both temperature and flow data make MR scanning an attractive option for interventional/intraoperative imaging [14]. The idea of using MR imaging for real-time interventional/intraoperative guidance was first explored using a mid-field strength (0.5 T) system at the Brigham and Women's Hospital in Boston in collaboration with General Electric Medical Systems (Milwaukee, Wisconsin, USA). The results were first published in 1997 [20]. Since then, real-time MR imaging has been used by a number

of centres to guide and monitor various invasive and non-invasive interventions including diagnostic biopsies, thermal therapies (including interstitial laser therapy and cryotherapy), vascular procedures (such as stent placement, aneurysm obliteration, and arteriovenous malformation resection), removal of epileptogenic cortex, brain tumour resection, cyst drainage, nephrostomy, cholecystostomy, laminectomy, and prostate procedures [37-39]. The purported advantages of interventional/intraoperative MRI include excellent soft tissue contrast; increased surgical precision and resection control; a lower likelihood of reoperation; and the ability to visualise tissue changes, such as brain shift, and acute complications in real-time as surgery proceeds.

The use of real-time MR imaging to facilitate minimally invasive therapeutic procedures, such as biopsies and cyst drainage, is referred to as interventional MR imaging whereas guidance to facilitate open surgical procedures, such as lesion resection via craniotomy, is usually referred to as intraoperative MR imaging. For the sake of clarity, this report will follow these generally accepted definitions and use the acronym of IMRI when referring to interventional/intraoperative MR imaging collectively.

Design

The design of an IMRI system is an exercise in finding the optimum balance between the opposing requirements of access to the patient and magnetic field strength, i.e. image quality. Conventional diagnostic MR imagers have relatively high contrast resolution and fast imaging, as well as sensitivity to temperature and flow, conferred by their closed design, which enables the generation of a homogeneous, high strength magnetic field. However, this design does not allow access to the patient during a scan. On the other hand, a more open design and lower magnetic field strength compromises image quality and increases imaging time [12, 33, 37].

MR imaging can be used to monitor or guide a procedure, or both, and this choice will affect the final system design. Monitoring surgical progress and tissue changes, and confirming the accomplishment of the surgical goal can be achieved with intermittent imaging performed at pre-determined points during the operation. Consequently, a slightly modified conventional diagnostic scanner can be used for this purpose because access to the patient is not a necessity. However, the requirements for continuous real-time MR guidance of surgical tools, such as biopsy needles, endoscopes, or laser fibres, throughout a procedure demands more sophisticated modifications to the MR imaging system [33, 40].

Interest in IMRI has flourished, resulting in a variety of different commercially available imaging systems. These can be subdivided into three categories according to how the system deals with the problem of accessing the patient during the procedure [39].

Moving the patient to the magnet

Short bore magnets

The most obvious way of resolving the conflicting needs of the operative and MR imaging environment is to keep them separate but in close vicinity. These IMRI systems have a closed short bore 1.5 T superconducting magnet with a heavily shielded fringe field. The patient is operated on outside the 5 gauss line, but when imaging is required the customised operating table slides the patient into the bore of the magnet [12, 28, 33]. Biopsies can be performed while the patient is in the scanner, provided that all ferromagnetic material has been removed, by using an extended mechanical arm and an MR compatible microscope [12]. Siemens Medical Systems (Erlangen, Germany) and Philips Medical Systems (Best, The Netherlands) produce 1.5 T systems based on this design.

This high field system has an excellent signal-to-noise ratio and provides standard MR capabilities such as MR spectroscopy, MR angiography, MR venography, diffusion weighted imaging, chemical shift imaging, thermal monitoring, and functional imaging [28, 33]. However, this design does not allow interactive real-time guidance of procedures because only intermittent imaging can be performed. The use of navigation systems can be cumbersome and repeated imaging can significantly add to operative time [12]. Patients weighing more than 150 kg or who need to be operated on in the lateral or prone position may not fit in the bore. In addition, the anesthesiologist is unable to directly observe or access the patient during a scan [28, 33].

Moving the magnet to the patient

High field systems

The other way of maintaining a demarcated operating and imaging environment is to move the magnet rather than the patient. Innovative Magnetic Resonance Imaging Systems (IMRIS) (Winnipeg, Manitoba, Canada), together with the University of Calgary, produced a closed bore 1.5 T superconducting magnet that is 1.3 metres long and has a 92 cm diameter bore (72 cm with 23 nT/m^2). The system is actively shielded by a secondary magnetic coil of opposite polarity that is situated outside the main magnetic coil. This substantially reduces the magnetic fringe field. The ceiling mounted magnet is housed in a docking bay next to the operating theatre. When imaging is required, the magnet is moved along rails into the operating room by a small electric motor. The cantilevered operating table, constructed of stainless steel, plastic, fibreglass, and brass, has a hydraulic system that allows rotational and vertical movement in any direction. The patient's head is immobilised during neurosurgical procedures with a three or four pin carbon filament head holder that is mounted to the bottom half of the radiofrequency coil. Radiofrequency shielding during imaging is achieved by enclosing the operating table in a copper impregnated fibreglass tent,

which is connected to the magnet with a silver impregnated mesh collar. The magnet now includes a body coil that allows imaging of the entire body. An imaging procedure takes between 15 and 35 minutes [6, 12, 33, 41, 42].

This imaging system offers better patient access in an emergency than fixed magnet designs and can be moved out of the operating room when not in use [6]. It thus allows sharing of the technology between medical disciplines, such as surgery and diagnostics. The stationary operating table means that anesthetic monitoring and patient safety are not compromised during the imaging process. However, all MR incompatible instruments must be removed from the patient prior to imaging. Patients can be imaged in the prone, lateral, or supine position but current use has been restricted to patients who weigh less than 150 kg. The lack of surgeon access to the patient during imaging precludes real-time guidance of procedures [6, 28, 43, 44].

Low to mid-field systems

Odin Medical Technologies (Yokneam, Israel) manufacture a small semi-portable 0.12 T open configuration imaging system (PoleStar™ N-10) comprising a pair of vertical ceramic permanent magnets that are 40 cm in diameter and spaced 25 cm apart. The scanner can be swung out of the way on a pair of trunnions when not in use. The magnet is housed in a cast iron compartment, which shields the magnet, and can be stored under the operating room table or rolled out of the surgical area. A benefit of the low field strength is that surgical instruments do not need to be MR compatible. However, the low field strength is also the main drawback since it results in a longer scan time, lower image resolution, and a limited field of view, which can be problematic for large or deep seated lesions [12, 28, 33]. Adequate access to lateral or posterior lesions is not always feasible since it is dependent on the weight, neck length, and shoulder width of the patient [45, 46].

Operating within the magnet

Biplanar configuration

Most interventional and intraoperative imaging to date has been performed in magnets with a biplanar configuration. In this design, the patient is positioned between two flat magnetic poles that are configured either horizontally or vertically. These systems typically use lower field permanent or resistive magnets with field strengths ranging from 0.064 to 0.3 T, but superconducting mid-field models have also been manufactured. However, their image quality is substantially less than high field cylindrical systems [9, 12, 33].

The degree of access to the patient depends on the configuration of the supports that separate the two magnetic poles. Siemens Medical Systems have developed a C-arm design (Magnetom Open) where a single column on one side supports the upper magnetic pole, thereby allowing side access to the patient from the remaining open area

of the circumference. Other manufacturers produce systems with two or four supporting posts, which have a slightly more restricted patient access. Another version has an operating table where the head end swings out of the magnet to allow full access to the patient when imaging is not required [12, 33]. Interventional procedures, such as biopsies, can be performed within the magnet, but not surgical operations. In addition, any procedure that requires a vertical or oblique approach may not be possible with large patients because of the small gap between the magnetic poles [33]. However, vertical access can be achieved with a biplanar magnet by installing a horizontal gap biplanar magnet on its side to yield a vertical gap of 47 cm between the magnetic poles [9, 12].

Double donut configuration

The double donut configuration is a hybrid of the open bore biplanar and closed bore cylindrical designs. The 0.5 T Signa SP system produced by General Electric Medical Systems (Milwaukee, Wisconsin, USA) comprises two very short superconducting cylindrical magnets arranged vertically and separated by a 56 cm gap. The imaging isocentre of the magnet is located in a 30 cm diameter spherical volume in the centre of this gap. The operating table can be positioned in the magnet either in the conventional manner along the length of the bore or transversely through the vertical gap. The system can also accommodate procedures that require patients to be in a sitting position. Thus, the patient can be accessed from the side or from above while positioned within the magnetic field. The near real-time MR images are displayed on monitors positioned within the gap above the operator's head [9, 12, 47].

This system has a large fringe field and requires all instrumentation to be non-ferromagnetic. In addition, the open configuration of the magnet complicates the engineering of the radiofrequency coil so that a flexible transmit receive coil has to be secured to the body with Velcro straps. This provides only a limited field of view. The mid-field strength results in longer imaging times, lower spatial resolution and signal-to-noise ratio, increased image distortion, and limited functional and physiologic capabilities, but provides sufficient detail for guiding interventions [12, 28, 33, 48].

Navigation methods

The development of MR compatible operating microscopes and surgical instruments has meant that most IMRI systems have an integrated frameless stereotactic navigation system that allows updating of preoperative image maps as surgery proceeds. Tracking is usually achieved optically, with infrared light reflecting spheres or light emitting diodes, or by means of miniature coils attached to the instruments that are visible on MR images. However, the requirements of IMRI are different to those of diagnostic MR imaging, and novel pulse sequences are needed to achieve the right balance between image contrast and speed of acquisition. At each step of the procedure, the temporal, spatial, and contrast resolution requirements are different, and image artifacts produced

by probes or needles in the viewing field further complicate this. This area is likely to undergo extensive development in the near future [33, 40, 49].

Regulatory status and cost

The 1.5 T systems currently available are: BrainSuite by BrainLab (Westchester, Illinois, USA) and Siemens Medical Systems (Malvern, PA, USA), Neuro II by IMRIS, and Gyroscan by Philips Medical Systems. Three systems are available in the low to mid-field strength range: PoleStar™ N-10 by Odin, Signa SP by General Electric Medical Systems, and Magnetom Open by Siemens Medical Systems [50].

The first IMRI system was cleared for marketing through the United States Food and Drug Administration (FDA) 510(k) program in 1995. As of July 2003, five manufacturers marketed one or more FDA-cleared IMRI systems [50]. General Electric, Siemens, and IMRIS also hold medical device licences (class 2 or 3) from Health Canada for their IMRI systems.

IMRI systems can range in cost from approximately US$1 million for a small dedicated system to over US$6 million for a complete neurosurgical suite that comprises a high field magnet, MR compatible instrumentation, an integrated neuronavigation system, and installation [50, 51]. In addition to the purchase price of the magnet, the cost of constructing a facility to house an IMRI unit ranges from US$700,000 to US$1 million, plus additional costs for structural support and radiofrequency shielding. Renovating an existing facility to accommodate a smaller IMRI system costs approximately half that. The ongoing service cost for an IMRI system is approximately 5% to 10% of the purchase price per year [50].

COMPARATIVE EVIDENCE ON THE SAFETY, EFFICACY, AND COST OF IMRI

Safety and efficacy/effectiveness

Published evidence

A tabulated summary of extracted data from selected studies is provided in Appendix A. The search strategy and study selection criteria are outlined in Appendices B and C. Only four non-randomised comparative studies met the inclusion criteria.

Interventional MR Imaging

One study [52] retrospectively compared brain biopsy in 157 patients performed with either a 1.5 T IMRI unit or a conventional stereotactic technique that used CT or MR images for guidance. Snapshot MR scans were performed throughout the interventional MR procedure and also at the end of the biopsy. The diagnostic tissue yield was similar between the two techniques, even though an intraoperative pathology examination was performed on all tissue retrieved with interventional MR but on only 93% of biopsy samples obtained with the stereotactic procedure. One patient who underwent stereotactic biopsy suffered a fatal hemorrhage, whereas no deaths occurred after the interventional MR technique. The morbidity rates were similar between the two treatment groups. On face value, these results suggest that interventional MR imaging is safer and more effective than stereotactic brain biopsy, but the results were not confirmed statistically. In addition, no baseline patient information was provided and other important variables such as lesion size, type, and location were not controlled for. This makes it impossible to judge whether the results were confounded by an uneven distribution of confounding factors between the two treatment groups.

Intraoperative MR Imaging

Two studies [44, 53] compared craniotomy for tumour resection performed either with or without high field 1.5 T IMRI. Archer et al. [44] analysed retrospective data from the first 76 case matched patients at the University of Calgary, 93.4% of whom correlated on at least three out of five of the match criteria. MR imaging was used intermittently throughout the surgical period, but three quarters of the patients only had two imaging sequences performed, one prior to incision and a quality assurance scan before wound closure. No details of the conventional resection procedure were provided. There was no significant difference between the two groups with respect to preoperative parameters such as gender mix, age, weight, hemoglobin level, or American Society of Anesthesiologists (ASA) score ($p < 0.05$). The operative time for intraoperative MR patients was an average of 122 minutes longer (mean total time of 407 minutes) than for the conventional group (mean total time of 285 minutes), with intraoperative MR

imaging being directly responsible for 83% of this difference. However, the longer operative time had no discernible effect on perioperative anesthetic outcomes such as patient recovery, blood loss, or transfusion and fluid requirements. In terms of safety, no treatment failures or postoperative infections occurred in either treatment group. Unfortunately, no details were provided on what types of tumour were resected, so it was unclear whether they presented a high or low degree of technical difficulty with respect to proximity to critical brain areas or identifying tumour margins. Since the focus of the study was limited to perioperative anesthetic outcomes, no data were available on the effect that intraoperative MR imaging had, if any, on completeness of resection and postoperative outcome.

Hall et al. [53] conducted a cost-effectiveness study on data from 47 patients who were case matched by diagnostic code. Hospital stay was significantly shorter for adult patients in the intraoperative MR group, compared to the conventional group, regardless of whether they were undergoing craniotomy for initial or repeat resection. However, the length of hospital stay was only significantly reduced for pediatric patients who required an initial resection. None of the intraoperative MR patients who had initial resection of a tumour required subsequent surgery during the follow-up period, which ranged from 3 months to just over two years. In contrast, 30% of adults and 20% of pediatric patients in the conventional treatment group required reintervention after a mean interval of 9.3 and 13.3 months, respectively.

The main focus of the study by Gralla et al. [54] was to compare the clinical applicability of three different frameless stereotactic navigation systems in 26 patients undergoing resection of supratentorial cavernous hemangiomas. However, 14 of these patients also had intraoperative MR resection control images taken prior to wound closure with a 0.2 T scanner. Since raw data for some of the postoperative outcomes were reported for all 26 patients, a secondary analysis of comparisons between the intraoperative MR and conventional group was performed. This was considered valid since the study found no difference between the three navigation procedures in terms of preoperative image registration or clinical applicability. Complete resection of the hemangioma was achieved in both the intraoperative MR (assessed intraoperatively) and the conventional group (assessed by postoperative MR imaging), and no major morbidity or mortality occurred in either patient group. The proportion of patients who were completely free of seizures after surgery was similar in both treatment groups. However, only half as many patients experienced clinical improvement in the intraoperative MR group, compared to the conventional group, and 14% of patients had a worsening of symptoms after the intraoperative MR surgery. No such deterioration was observed after conventional surgery.

All of the included studies analysed the results of their first experience with IMRI. Therefore, even though these studies are comparative, they are really only one step up

from a feasibility study. Given the level of technological complexity involved in applying an IMRI system, it is likely that learning curve effects have significantly confounded these results such that they may underestimate what can be achieved with IMRI, particularly in terms of operative time. However, the quality of case matching was poor, and three studies [52-54] did not attempt to control for established prognostic factors such as seizure history and lesion location. In addition, the studies were retrospective and it was often unclear whether surgical, anesthetic, or postoperative management was standardised between the IMRI and conventional procedure groups. Therefore, bias is likely to be rife in all four studies and it is impossible to delineate whether this tended to the underestimation or overestimation of the effectiveness of IMRI.

Unpublished evidence

Intraoperative MR Imaging

A retrospective analysis of 30 patients who underwent surgical removal of high grade gliomas was reported in an industry publication produced by Siemens AG (Erlangen, Germany) [55]. Although the authors appeared not to be directly affiliated with Siemens, it was unclear to what extent the publication was peer reviewed, or if the authors received any form of compensation for the article. In addition, the IMRI system used in the study was a Siemens 0.2 T Open MR scanner. Thus, any data derived from this publication should be treated cautiously because it is possible, though not certain, that only studies employing Siemens equipment and reporting positive outcomes are accepted for publication.

Fifteen patients undergoing intraoperative MR guided tumour resection were matched for tumour size, location, and overall complexity with fifteen patients who underwent conventional tumour resection with BrainLab (Heimstetten, Germany) neuronavigation. Complete tumour resection was achieved in 47% of the intraoperative MR patients, whereas only 20% of patients in the conventional group had a comparable result. The proportion of residual tumour in the other eight intraoperative MR patients was, on average, much smaller (mean 2.4%) than in the 12 patients treated with conventional methods (mean 21.2%). These results were presented in an anecdotal manner so there was very little detail provided on surgical technique or patient management. It was also not clear how successful the matching process was since no comparison of preoperative parameters was reported.

Cost comparisons

Published evidence

Intraoperative MR Imaging

Only one published study reported any cost comparison data. Hall et al. [53] conducted a cost comparison study by retrospectively analysing hospital financial and information systems data. They case matched 47 consecutive patients undergoing brain tumour resection with high field 1.5 T IMRI by diagnostic code with patients undergoing tumour resection with an unspecified conventional operative procedure. The study used tumour reintervention rates and length of hospital stay to establish effectiveness parameters for the two procedures, but only the latter was incorporated into the cost analysis.

The mean total hospital cost for an adult to undergo an intraoperative MR procedure or conventional procedure was similar, regardless of whether it was an initial or repeat resection. However, the total hospital cost was nearly halved for children having an intraoperative MR procedure. The cost to charge ratio for first resections in adults was 69.6% with intraoperative MR imaging and 71.4% for conventional surgery. There was no difference for repeat resections. For pediatric patients, the cost to charge ratio was 71.4% for an intraoperative MR first resection and 74.8% for conventional treatment. For repeat resections these ratios were 72.8% and 73.9%, respectively. The authors suggested that the lower cost to charge ratios for intraoperative MR procedures have the potential to increase the per patient hospital revenue. However, there was no statistical analysis reported for these comparisons so it is unclear whether the differences were statistically significant. This cost analysis was rather simplistic and did not include factors such as postoperative imaging and medication requirements. The rate of repeat resection was reported, but the zero rate of reintervention in the intraoperative MR group does not necessarily mean that the tumours had not recurred, since a tumour may have returned but not yet be serious enough to warrant reoperation. In addition, no details were provided on the type of tumours resected so it was not clear what level of technical difficulty was represented in the patient groups. The time span of the costing study was disparate between the intraoperative MR and conventional surgery group, with the latter spanning a period from 1993 to 1998 while intraoperative MR imaging was only analysed from May 1997 to June 1999. This rendered the comparison dubious because of the inevitable confounding changes that occur over time with respect to costs, operative methods, resource utilisation, and postoperative management protocols.

Unpublished evidence

Intraoperative MR Imaging

Rubino et al. [55] provided an anecdotal comparison of 32 patients who underwent intraoperative MR guided tumour resection and 32 patients who had conventional tumour resection performed with BrainLab neuronavigation from 1998 to 2000. The variable direct costs and duration of hospital and intensive care unit stay were similar for the two groups. The average operating time was 9.5 hours for the intraoperative MR technique, which was 41% longer than the time it took to perform the conventional procedure. This difference was the main contributor to the extra US$727 in variable direct costs incurred by intraoperative MR imaging. No statistical analysis of the data was reported and there were no details provided on patient selection, tumour type, preoperative patient parameters, or surgical procedure. The authors reported that the total MR imaging time over the first 100 patients dropped from two hours to less than thirty minutes per procedure. However, it was not clear at which end of the learning curve the 64 patient in the cost comparison were situated. Nevertheless, it is probable that the intraoperative MR results were confounded by a learning curve effect.

Ongoing research

A number of phase II trials are currently being conducted to assess the feasibility of IMRI. The Centre Hospitalier de l'Universite de Montreal is collaborating with the Mayo Clinic Cancer Center in Minnesota in an industry sponsored study to assess the use of MR guided focused ultrasound in the treatment of breast cancer. The National Cancer Institute in the United States is funding two studies, one on MR guided brachytherapy for prostate cancer and another, in partnership with the Ireland Cancer Center, on MR guided radiofrequency ablation of primary kidney cancer, liver metastases, and other solid tumours. A feasibility study is also being conducted in the United Kingdom to assess the use of MR imaging to guide interstitial laser treatment for breast and prostate cancer.

The University of Calgary is working in conjunction with MD Robotics (Brampton, Ontario, Canada) to develop an MR compatible robotic system for neurosurgical procedures. Similar developments are taking place at the Brigham and Women's Hospital in Boston, USA. Multiple modality intraoperative procedures that combine MR imaging with endoscopy and ultrasound are also under investigation [50].

UTILISATION OF IMRI

Within Canada [49]

Calgary, Alberta

The Seaman's Family Research Centre at Foothills Hospital is a demonstration site for a 1.5 T mobile closed bore ceiling mounted MR scanner that is now manufactured by IMRIS, a spin-off company of the National Research Council's Institute for Biodiagnostics. This system is used for preoperative surgical planning, confirming the accomplishment of surgical objectives, and detecting intraoperative complications such as hemorrhage and ischemia. As of May 2000, the Neuro II MR scanner has been used in approximately 400 operations involving children and adults to treat pathology that covers the full spectrum of neurosurgery, including disorders of the cervical spine. The magnet and console are now supplied by Siemens through a partnership with IMRIS.

Winnipeg, Manitoba

The Andrei Sakharov MRI Facility at the St Boniface Research Centre has a 0.2 T Siemens Open C-shaped biplanar MR scanner. The system is currently used as a research tool for exploring robot guided laser surgery. A prototype ceramic robot is currently in development and investigators are also studying ways of using MR imaging to control the distribution of laser energy deep within the body. The aim is to apply this technology to the treatment of herniated lumbar disks and eventually to liver tumours.

Quebec City, Quebec

The Hôpital Saint-François d'Assise has a 0.5 T double donut General Electric IMRI that was installed four years ago. The system was initially used for research on cryotherapy of spine, breast, and liver lesions, and spinal cryotherapy interventions now comprise 90% of all procedures. The equipment is used two days a week for interventional procedures, with a total of 15 patients being treated. In order to maximise the utilisation of the IMRI, the hospital intends to expand practice to 5 days per week and increase capacity to 40 patients.

Toronto, Ontario

The Toronto Western Hospital has a low field 0.24 T biplanar MR scanner from General Electric that has been installed on its side to provide vertical access to the patient during imaging. This system is augmented with an integrated image guidance and robotic surgical system that was developed in-house. The scanner is primarily used for brain and some spine surgery. However, there is a plan to replace this unit with a very high

field 3.0 T IMRI system in the next year. If this is approved, the utilisation will shift to a combined interventional/intraoperative program.

Halifax, Nova Scotia

The Brain Repair Centre, which is part of Dalhousie University and Queen Elizabeth II Health Sciences Centre, does not currently have an IMRI system. However, a new Neuroimaging Research Laboratory was completed in June 2003 to house a team of researchers and technologists sponsored by the Institute for Biodiagnostics. The Brain Repair Centre is considering the purchase of a mobile IMRI system, similar to the one in Calgary, with funds provided by the Atlantic Innovation Fund, which is a five-year federal government initiative administered by the Atlantic Canada Opportunities Agency. This will augment the Centre's research on using stem cells to treat brain disorders and repair spinal cord injury.

Ottawa, Ontario

The University of Ottawa Heart Institute has applied to the Canadian Foundation for Innovation for an IMRI system, to be supplied by IMRIS, for use in cardiology. The decision is pending.

Worldwide

Approximately 40 IMRI systems were installed worldwide at the beginning of 2003 [50]. The main suppliers of these systems are currently Siemens, General Electric, Philips, IMRIS, and Odin [49]. However, distribution appears to be uneven, with multiple sites existing in Canada and the United States while other countries, such as Australia [12], have no IMRI systems.

DISCUSSION AND CONCLUSIONS

Efficacy/effectiveness of IMRI

The results of the included comparative studies were sketchy. There was hardly any overlap in the perioperative and postoperative outcomes reported by the studies, so only an incomplete mosaic of trends can be constructed from the data. The results of one study [52] suggested that interventional MR imaging for guiding brain biopsy produced similar diagnostic tissue yields, compared to a conventional stereotactic method, but it was not reported whether the length of the biopsy procedure differed between the two techniques.

Using intraoperative MR imaging to monitor brain tumour resection resulted in a substantial increase in operative time, compared to conventional surgery, but with no discernible effect on the perioperative anesthetic outcome of patients [44]. Conversely, the hospital stay was generally shorter after the intraoperative MR procedure. The use of intraoperative MR imaging for resection control of supratentorial cavernous hemangiomas made no difference to the amount of pathology resected [54], compared to standard neuronavigation techniques, whereas significantly more tumour volume was resected in patients with high grade gliomas [55]. Unfortunately, no postoperative outcomes were reported for the latter patient group. One study [53] that did report reintervention rates, which were higher for the conventional surgery group compared to the intraoperative MR group, did not report the degree of brain tumour resection achieved. Another study that reported complete resection for both treatment groups [54] observed lower rates of clinical improvement for the intraoperative MR group, compared to the patients who underwent conventional surgery. However, these results were confounded by an uneven distribution of prognostic factors between the two treatment groups. Thus, it was impossible to determine from this patchy evidence whether the increased resection potentially achieved with the intraoperative MR procedure has any beneficial effect on postoperative outcomes.

All of the included studies presented data that encompassed the author's first experiences with using IMRI technology. Consequently, these results may underestimate the capabilities of IMRI because of substantial confounding from the learning curve effect, but the presence of methodological flaws in the studies made it impossible to characterise the overall magnitude or direction of these biases. Thus, it is unclear whether the equivocal results are a consequence of limitations in study design, the IMRI procedure itself, or both. The included studies only used IMRI as a tool to guide or monitor interventional and operative neurosurgical procedures. Therefore, it remains unclear what the clinical utility of IMRI may be when it is used to guide or monitor any other type of intervention or surgery.

Safety of IMRI

Patients who underwent interventional MR image guided brain biopsy had similar postoperative morbidity rates to those who underwent a stereotactic technique. However, one fatality occurred following conventional stereotactic biopsy, whereas no deaths occurred in the interventional MR group. Unfortunately, the widely disparate sample sizes of the two patient groups, as well as other biases inherent in the study design, meant that these results were not definitive. Thus, it remains unclear whether interventional MR imaging is safer than stereotactic techniques for conducting brain biopsy.

None of the included studies reported any adverse events directly related to the use of intraoperative MR imaging. However, this was also true for the conventional procedures that intraoperative MR imaging was compared to. It is unclear from the evidence whether patients undergoing an intraoperative MR procedure are at a higher risk of adverse events as a result of the longer operative time. Over four hundred patients have now undergone a craniotomy for tumour resection with intraoperative MR imaging at the University of Calgary. So far, the craniotomy procedure has been aborted in four patients because intraoperative MR images taken after the induction of anesthesia, but prior to scalp incision, had shown considerable lesion regression, which obviated the need for surgery. Consequently, intraoperative MR imaging is potentially important in updating preoperative diagnostic images (Dr. G. Sutherland, personal communication).

Some IMRI systems require the patient and the surgeon to be within a high magnetic field for prolonged periods. In addition, the radiofrequency pulse of the MR scanner can induce currents in electrical cords and medical devices, such as rectal temperature probes, which can cause burns if they are in direct contact with the patient's body [56, 57]. Data on the effects of magnetic or radiofrequency fields on biological tissue are limited, and there have been few human studies conducted. Current Canadian guidelines suggest that the health hazard of being exposed to static magnetic fields of less than 2 T is minimal. The effects of exposure to higher magnetic fields are unknown [58]. What implications this may have for very high field IMRI systems currently being developed is unclear.

Economic implications

One limited cost comparison study [53] suggested that an intraoperative MR procedure for brain tumour resection performed at a university medical centre generated similar or lower hospital costs than a conventional procedure, and was associated with a generally lower cost to charge ratio. The study also reported a shorter hospital stay and lower rates of repeat resection for the intraoperative MR patient group, but these outcomes do not necessarily translate into improved net health outcomes or quality of

life. An unpublished study [55] reported that intraoperative MR imaging resulted in only a slight increase in hospital direct costs in spite of having a much longer operative time. However, these costings were based on the US and German healthcare systems, so the applicability of these results to the Canadian system is tenuous. There are many difficulties in comparing cost analyses due to the effects of differences in institutional accounting methods; teaching versus non-teaching centres; the ratio of cost to charge in for-profit hospitals; the inclusion of physician fees or perioperative costs; and patient specific factors such as the number and size of tumours requiring resection [59, 60]. In addition, factors such as hospital length of stay are variable and often strongly influenced by reimbursement structure and postoperative care protocols.

There is continued speculation in the literature as to whether IMRI, with its high setup costs and ongoing maintenance fees, improves patient outcomes enough to justify the expense. On the basis of this review, such questions cannot be answered by the available evidence. It has been suggested that if the MR scanner used for IMRI is also used for pre- and post-operative imaging studies in conventional procedures, the overall costs of IMRI will be somewhat offset [33]. However, the weakness of this idea may be in the logistics of tying up a high cost specialised MR scanner on more routine imaging tasks. In addition, if a cheaper imaging technology like CT or ultrasound is routinely used in conventional operative procedures, it then becomes more of an issue to justify the extra expense of an IMRI unit. Since the included studies provided few details on the comparator procedure, it was unclear whether IMRI required a surgical team that differed in size or skill mix from that of a conventional procedure.

Some centres have sought to offset the cost of acquiring an IMRI system by operating a twin suite whereby the scanner is shared between an operating room and an interventional or diagnostic suite [33, 61], and manufacturers are starting to specifically design dual use MR imaging suites to facilitate this. Initially there were concerns that this would pose a problem for infection control during invasive procedures, but early results from centres with dual use suites suggest otherwise [61, 62]. However, the multidisciplinary utilisation of IMRI in this way may prove challenging.

Another aspect of cost that is sometimes overlooked when purchasing sophisticated equipment is that rapid advances in technology will mean that units quickly become obsolete. Thus, the purchase of an IMRI system commits the buyer to continuous upgrades if the system is to remain state-of-the art. This upward developmental trajectory makes it difficult to assess the utility of current IMRI systems because they are a rapidly moving target.

Further considerations

Indications for the use of IMRI

Interest in intraoperative MR imaging has been propelled by the desire of neurosurgeons to understand the effect of surgery on both the lesion and the brain, with the aim of ultimately improving patient outcome. Consequently, all of the comparative studies conducted on IMRI to date have been in the field of neurosurgery. However, it is likely that intraoperative MR imaging may not be indicated for all neurosurgical procedures, particularly in cases where the extent of resection has no demonstrable effect on patient outcome. Most brain tumours, aneurysms, and vascular malformations can be safely treated with current microsurgical techniques in conjunction with either frameless or frame-based stereotactic navigation [33]. In addition, stereotactic navigation may be more than adequate for removing brain tumours that are smaller than 20 cm [3, 63].

Intraoperative MR imaging is likely to be of greatest value when tumour borders cannot be distinguished from normal brain tissue with the naked eye, particularly when they infiltrate vital parts of the brain such as the motor strip [62]. Current published experience suggests that intraoperative MR imaging may be valuable in procedures for ventricular tumours, epilepsy, pituitary tumours, and disorders of the cervical spine [43, 64]. Other potential indications include lesions that are difficult to approach or are situated in the vicinity of sensitive cortical areas; small lesions that might be hard to visualise during surgery; and recurrent tumours [10].

In the case of malignant neoplasms, as many as 80% of procedures leave some tumour behind [10, 65]. Resection of high grade gliomas is particularly problematic because tumour cells are often present in the neuropil well beyond what is visible even on conventional MR images [20, 41], so it is questionable whether intraoperative MR imaging in its current form can really achieve complete resection. While the extent of resection of low grade gliomas appears to affect disease progression and survival, the evidence for high grade glioma resection is more equivocal [46, 65]. In the latter case, if complete resection is of little benefit compared to subtotal resection, then surgery is only palliative and there is no need for intraoperative MR imaging since subtotal resection can be achieved by an experienced neurosurgeon with conventional guidance methods [62]. A similar controversy surrounds the effect of resecting the hippocampus and amygdala on epileptic seizures [36, 66]. In these instances, it is imperative to assess what effect removing slightly more tissue with intraoperative MR imaging has on patient outcomes, compared to that which can be achieved with conventional techniques [20, 41].

Another reason for using intraoperative MR imaging is to compensate for brain shift. However, this is not always a problem in surgery, particularly during short procedures

or when brain manipulation is minimal. Also, some patients are more prone to brain shift than others [61, 67]. Thus, intraoperative MR imaging may not be needed routinely. It is also debatable whether multiple resection controls during all procedures are necessary [22, 36].

Exposure to an MR scanner is potentially fatal for patients with implants such as aneurysm clips, pacemakers, or infusion pumps and can cause serious damage in patients with metal remnants in their body from previous injuries [57]. The procedure is also contraindicated in patients at risk of myocardial ischemia because diagnostic ST-segment measurements cannot currently be monitored with an electrocardiogram while a patient is in the fringe field of the magnet [29, 68]. Some patients may also be ineligible for the procedure because their size or the position required to access to the lesion cannot be accommodated within the IMRI unit.

The relatively recent development of IMRI means that it is probably too early to consider IMRI solely as a clinical tool since its capabilities and limitations are unknown. Thus, it is not yet possible to establish a definitive list of indications for the use of IMRI. However, this should be a future goal since it has the potential to maximise the efficient utilisation of the technology by identifying those patients who would receive the most benefit from IMRI [61]. For example, ultrasound provides better real-time visualisation of arteries, fluid filled tissues, and calcifications, and may be more appropriate to use in patients with cystic lesions than IMRI [69]. In cases where the appropriate management of a lesion is uncertain, the use of IMRI will also remain unclear.

The spectrum of procedures that have used IMRI extends beyond neurosurgery to include percutaneous biopsies; endoscopic surgery of the abdomen, sinuses, and spine; resection of liver pathology; cryogenic or percutaneous interstitial thermal therapies; and brachytherapy of the prostate [57]. However, the utility of interventional MR imaging is also unclear because of the absence of comparative studies.

Technical considerations

The application of MR imaging to the interventional/intraoperative setting is still in its infancy. Currently, there is a choice between user friendly systems with limited imaging capabilities and systems with versatile imaging but limited operating room functionality [16]. Some procedures do not require continuous imaging while others do, and it is still not clear whether the optimum use of IMRI will be in resection control and monitoring or providing real-time guidance during procedures. Consequently, the ideal IMRI setup has yet to be developed, and it is likely that different systems will be developed to meet the individual needs and budgets of users [33]. Further developments in other imaging and navigation methods may also affect this.

High field MR scanners provide a greater variety of imaging sequences than low and mid-field systems, but whether these can be successfully applied intraoperatively has

yet to be investigated. New pulse sequences that are distinct from those used for diagnostic imaging and are less susceptible to artifacts need to be developed [64, 70]. Further work is also needed to establish the appropriate timing and dose rates for administering contrast agents such as gadolinium [61, 62].

In its current form, IMRI has some limitations. New designs are needed that minimise disruption to established neurosurgical, anesthetic, and nursing techniques [41]. The restrictions imposed by the magnetic pole gap on workable operating space and patient size, positioning, and monitoring also need to be resolved. IMRI systems currently require extensive room modifications including radiofrequency shielding and sometimes structural alterations to accommodate the weight of the unit. In addition, many systems require MR compatible tools and instruments because standard medical grade stainless steel tools can become dangerous projectiles in a magnetic field. Tools must be made from non-ferromagnetic materials such as ceramic or titanium, which reduces the range available and increases equipment costs [11, 57]. More often than not these tools are simplified versions of the original design that may not be amenable to standard sterilisation procedures and are less rigid, have fewer capabilities, and are less effective than conventional instruments [46, 47, 71].

The success of image guided interventions depends on the spatial and contrast resolution of the scanning device and its ability to demarcate normal and abnormal tissue [72]. However, as with all technology, the rate limiting step is often the human interface. It has been suggested that the widespread use of neuronavigation systems has highlighted their limitations because they are now available to surgeons with a broad range of skill levels [22]. Thus, it is possible that an average neurosurgeon with an IMRI unit may achieve results similar to those of a more skilled neurosurgeon without one [65]. However, this debate is somewhat spurious because the high cost of IMRI units and the complexity of integrating the system into the operative work flow will mean that they are not likely to be available in routine clinical practice any time soon. In addition, the more complex the imaging is, the greater the skill required to navigate in a three dimensional space that does not always have corresponding tactile feedback. Thus, an IMRI system is a useful adjunct to operative experience and anatomical knowledge, but is not a replacement for it. Even though some aspects of imaging can be automated, there is still a subjective component in the interpretation of the images by the surgeon or radiologist, and sound clinical judgement and surgical dexterity still appear to be pivotal in the overall success of IMRI procedures [38, 41, 70]. IMRI may actually require more sophisticated training to equip users with sufficient skills to competently handle the technology and a level of multidisciplinary training that was not previously required, which will have direct implications for the policies and future planning of training centres and accreditation bodies.

The future of IMRI

Research

The current research on IMRI is only just emerging from the stage of feasibility studies, which is to be expected given its relatively recent genesis. There are numerous case series studies documenting the use of IMRI in a variety of interventional and intraoperative procedures. Generally, these studies analyse the extent to which preoperative resection or biopsy goals were achieved in patients undergoing a conventional procedure. Thus, IMRI is used as a quality control to redirect further resection or biopsy until the operative goal is achieved. The percentage of patients whose preoperative plan was altered by IMRI is usually quoted as evidence of utility. However, without a comparator these studies can do little to answer questions on the efficacy of IMRI since there is no proof that the changes in the surgical plan made any difference to patient outcomes. In addition, operators may conduct surgery in a more conservative manner than normal if they know that they have a second chance at resection before the operation is completed [61].

Comparative studies are clearly needed to assess the benefit of this technology, particularly given its high cost. It is preferable, but not essential, that these studies have random allocation of patients to treatment groups. Well designed, non-randomised studies that match patients on the basis of prognostic factors, such as tumour location, can also be valuable. Comparative studies are not likely to be ethically problematic because most procedures that currently utilise IMRI have a well established alternative. Follow-up periods need to be long enough to adequately assess postoperative morbidity, recurrence rates, survival times, and quality of life according to the particular disease being treated and the primary goals of treatment.

Because the potential application of IMRI is so broad, there is no universal benchmark procedure. Thus, the comparator will be different for each indication; in spine surgery the comparator may be intraoperative CT imaging whereas for abdominal procedures it may be intraoperative ultrasound. It is imperative that the comparator technique is the most current, state-of-the-art version to ensure a bias free comparison. For example, the ultrasound scanners used in operating rooms are often out of date diagnostic machines that are clearly inappropriate to use in a comparison with a current IMRI system [35].

Some centres have developed enough experience that their learning curve has plateaued, and it is likely that more comparative studies will be forthcoming. In the meantime, it is important to establish databases of patients who have undergone IMRI procedures so that the experience can be used to formulate patient indication guidelines and establish whether there is a danger to patients or operators from prolonged exposure to the magnetic and radiofrequency fields generated during IMRI. In addition, since the risk associated with many conventional procedures that IMRI may

supplant is already quite low, it will take extensive data sets to demonstrate a further reduction in this risk [20]. It will also be important to establish what impact IMRI may have on case load.

Development

IMRI still has many limitations that require refinement. Many IMRI designs require movement of either the patient or the magnet during a procedure. This is inconvenient; increases operative time and the potential for contamination of the sterile surgical field; increases the likelihood of accidental disconnection or dislodgement of endotracheal tubes, anesthesia lines, monitoring devices, or surgical instruments within the operative field; and interrupts normal operative work flow [12, 42, 48]. The IMRI working environment can also be restrictive, since access to the patient is limited and the surgeon often has to operate in an uncomfortable, cramped position for long periods of time [11, 42].

Consequently, manufacturers are tinkering with system designs to try and meet the opposing needs of the imaging and operating room environment. Concepts such as a biplanar system in which the horizontal gap between the magnetic poles has been rotated 90° to allow direct vertical access, a head only superconducting C-arm design, and a biplanar 'flat bed' design with a very large magnetic pole gap are being explored in an attempt to increase patient access [73]. However, all of these concepts are based on low field magnets and will therefore suffer the problem of a decreased signal-to-noise ratio.

A major aim of future research is to incorporate modalities such as endoscopy and MR angiography, spectroscopy, and functional imaging into IMRI systems. Advances in data processing techniques may allow the fusion of multiple image data sets, even those derived from other techniques such as positron emission tomography. New pulse sequences are being developed to reduce imaging time and artifacts produced by MR compatible instruments, and some centres are already exploring the possibility of coupling IMRI with robotic technology [41].

There is currently a lot of interest in using MR imaging to monitor the effects of cryogenic ablation and thermal therapies, such as interstitial laser therapy, focused ultrasound, and radiofrequency coagulation. These techniques are generally most effective when the temperatures generated in the target tissue are maintained within a certain range, but this is notoriously difficult to achieve given the variability in tissue properties between patients. Using the temperature sensing capabilities of MR, it may be possible to monitor tissue effects and halt treatment once the desired thermal effect has been achieved [14, 74]. MR imaging may also be useful in monitoring the delivery of drugs and stem cell transplants into the body [75].

IMRI was originally in competition with conventional neuronavigation techniques. However, the recent integration of these navigation systems into IMRI units has changed this. It may be that IMRI will not replace other interventional/intraoperative imaging techniques but will become yet another option for selected patients undergoing procedures that require image guidance. IMRI is currently restricted to specialist interventional and surgical centres, and this is likely to remain the case in the foreseeable future.

Health policy implications

Given the current cost of most IMRI systems, it is important to decide whether the population density is such that the expense of an IMRI unit can be justified. The Seaman's Family Research Centre at Foothills Hospital in Calgary is the referral centre for all adult neurosurgical patients in southern Alberta, with between 800 and 1,000 elective or urgent craniotomies being performed annually. However, in a two year period from December 1997 to the end of 1999 only 80 patients underwent elective craniotomy using IMRI [44]. Thus, case load calculations must be based on a number of parameters including the type of IMRI procedures that will be performed, which could range from percutaneous interventions through to open surgery; the estimated need for these procedures in the local population; and the size of the subgroup of patients who have the appropriate indications and are actually eligible to undergo an IMRI procedure. Defining exactly which patients cannot do without this technology will not be possible until extensive experience has been accumulated.

The proximity of other centres with IMRI systems, as well as their current and projected future operating capacity, will also be major factors in determining technology placement. For Alberta, this would entail consultation with the Seaman's Family Research Centre in Calgary as well as canvassing interest among other main centres in Western Canada to determine the best site for further IMRI systems. Costs can potentially be reduced by using an IMRI system in a shared resource environment. This allows flexibility in that if the IMRI program does not prove cost efficient, the magnet can still be used for peripheral interventions or diagnostic scanning [61]. It has been suggested that if the rate of reintervention is reduced by using intraoperative MR imaging, additional patients can be treated with the resources that would otherwise have been used to treat recurrent disease [53]. However, this is currently counteracted by the significantly longer operative time for intraoperative MR imaging, compared to conventional procedures, which ties up personnel and equipment for longer periods and may even result in a decrease in patient throughput.

Care must be taken to ensure that a 'brain drain' of technical and medical expertise from one area to another does not occur as a result of the placement of an IMRI service. Currently, there is a shortage of skilled personnel, such as MR radiographers and engineers, in Canada. Advances in technology will only exacerbate this problem as

those with radiological expertise become 'knowledge centres' for medical colleagues in other disciplines [76]. Since these personnel are such an integral part of the IMRI procedure, the supply of technical staff is an important issue, particularly when IMRI units are in close proximity and may be in direct competition for the same limited pool of technical expertise.

IMRI is likely to diffuse slowly into the healthcare system over the next few years because of its inherent limitations, technological complexity, and cost. Consequently, it will likely remain a specialty procedure conducted by facilities with advanced interventional/surgical expertise and higher patient volumes [50]. This time lag provides an excellent opportunity for health managers to ensure that the future placement of IMRI scanners in Canada is both judicious and equitable.

The Bottom-line: IMRI is a high cost, developmental technology for which no major safety concerns have been identified to date. Due to its recent genesis, the scope, applicability, efficacy, and cost effectiveness of this technology have not been established. Concurrently controlled studies assessing the impact of IMRI on patient management and outcomes will provide the information required to resolve the question of whether IMRI has a broader clinical application beyond its current use in the research setting. As more IMRI systems are installed, such trials may become feasible.

APPENDICES

APPENDIX A: SUMMARY OF PUBLISHED COMPARATIVE STUDIES

Authors/ Location	Intervention	Study Design	Study Population	Results	Comments
Hall et al.[52,77] Minnesota, USA	**1) Stereotactic brain biopsy** Cosman-Roberts-Wells stereotactic system was used (Radionics, Burlington, Massachusetts, USA). Computed tomography (63.4%) and magnetic resonance (36.6%) guidance were used. Biopsies were performed using local anesthesia and intravenous sedation except in posterior fossa lesions or in young children where general anesthesia was administered. An intraoperative pathology examination was performed in 92.5% of biopsies. **2) IMRI procedure** A short bore 1.5 T magnetic resonance scanner (ACS-NT, Philips Medical Systems) was used for imaging. General anesthesia was used in all patients. Interactive scanning in two orthogonal planes was used during the procedure. An intraoperative pathology examination was performed in all biopsies. Imaging was also performed at the conclusion of the biopsy.	Retrospective non-randomised comparative study with historical controls. **Mean Follow-up:** Not stated **Setting:** University affiliated medical centre **Study Period:** **1)** February1991 to December 1996 **2)** January 1997 to June 1998 **Outcome Measures:** Rates of diagnostic tissue retrieval, morbidity, and mortality	**Sample Size:** **1)** 134 biopsies in 122 patients **2)** 35 biopsies in 35 patients **Patient Diagnosis:** Not stated **Mean Age:** Not stated **Gender Mix:** Not stated **Repeat Biopsies:** Not stated **Inclusion Criteria:** Not stated **Exclusion Criteria:** Not stated	Diagnostic tissue was obtained in all biopsies with IMRI, compared to 96.3% of samples obtained with the stereotactic procedure. **Mortality:** **1)** 0.8%; **2)** 0% **Temporary hemiparesis:** **1)** 0.8%; **2)** 2.9% **Wound infection:** **1)** 0%; **2)** 2.9%	Retrospective study design; historical controls; long study period for group 1. Treatment allocation was not random. It was unclear if the IMRI patients were consecutive. Anesthetic management differed between the two treatment groups. Lesion size, type, and location, were not controlled for. No baseline patient information was provided so it was unclear if confounding prognostic factors were evenly distributed between the treatment groups.

IMRI – interventional/intraoperative magnetic resonance imaging

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Authors/ Location	Intervention	Study Design	Study Population	Results	Comments
Archer et al. [44] Alberta, Canada	**1) Conventional operative procedure** No details given. **2) IMRI procedure** A mobile 1.5 T magnet resonance scanner (iMotion, Innovative Magnetic Resonance Imaging Systems) was used for imaging. Images were obtained intermittently during planned interruptions in surgery by moving the magnet over the patient. The BrainLAB VectorVision frameless stereotaxy system was used for surgical navigation (Heimstetten, Germany).	Retrospective non-randomised case matched controlled trial **Case Matching Criteria:** Lesion type (vascular versus tumour), pathology, location and size. **Follow-up:** Perioperative only **Setting:** University affiliated medical centre **Study Period:** December 1997 to December 1999 **Outcome Measures:** *Primary outcomes:* operative time, recovery score and body temperature on arrival in the PCAU, and length of stay in the post anesthetic care unit. *Secondary outcomes:* blood loss, intraoperative transfusion requirements and fluid administration, and characteristics of anesthetic management.	**Sample Size:** **1)** n = 76; **2)** n = 76 **Patient Diagnosis:** Elective craniotomy for tumour resection **Mean Age:** **1)** 49 years (SD ± 17) **2)** 45 years (SD ± 17) **Gender Mix:** **1)** M/F = 44 (57.9%)/32 (42.1%) **2)** M/F = 39 (51.3%)/37 (48.7%) **Repeat Resections:** **1) & 2)** 0% **Inclusion Criteria:** The presence of a lesion whose removal could be potentially enhanced by IMRI with respect to localisation and resection control. **Exclusion Criteria:** Contraindications to high magnetic field exposure; lesions requiring patient positioning other than supine or lateral; presence of coronary artery disease that requires ST segment monitoring with an electrocardiogram.	There were no treatment failures or postoperative infections in either treatment group. IMRI procedures were 122 minutes longer than conventional procedures. The average total time devoted to imaging was 101 minutes (SD ± 29). Imaging accounted for 83% of the difference in the length of the procedures. There was no difference in initial PCAU score, length of stay in PCAU, blood loss, perioperative transfusion rate, postoperative hemoglobin concentration, or intraoperative fluid administration between the two groups.	Retrospective study design. Treatment allocation was not random. Surgical and anesthetic management was not standardised. Lesion matching was imperfect due to lack of preoperative imaging for all patients. Anesthetic management differed between the two treatment groups. Did not address impact on postoperative patient outcomes. Patient inclusion for the IMRI group was dependent on whether a reasonable match could be found in the conventional group.

IMRI – interventional/intraoperative magnetic resonance imaging; PCAU - post anesthetic care unit; SD – standard deviation

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Authors/ Location	Intervention	Study Design	Study Population	Results	Comments
Gralla et al. [54] Erlangen, Germany	**1) Conventional operative procedure** Intraoperative frameless stereotactic guidance of tumour resection was achieved with a pointer based system (Stealth Station, Medtronic, USA) or a microscope based system using either the NC4 microscope or the Multiple Coordinate Manipulator (Zeiss, Germany). There was no significant difference between the three techniques with respect to registration accuracy or clinical applicability. **2) IMRI procedure** A 0.2 T magnetic resonance (Magnetom Open, Siemens Medical Solutions) was used. Images for resection control were obtained at the end of resection by moving the patient to the magnet.	Retrospective non-randomised comparative study (unclear whether controls were concurrent or historical). **Mean Follow-up:** **1) & 2)** 10 months (SD ± 6.8) (range 3 to 26) **Setting:** University neurosurgery clinic **Study Period:** July 1997 to July 2001 **Outcome Measures:** Operative outcome, completeness of tumour resection medication requirement, and complications.	**Sample Size:** **1)** n = 12; **2)** n = 14 **Patient Diagnosis:** Supratentorial cavernoma in a critical brain area **Mean Age:** **1)** 33 years (SD ± 17.1) (range 2 to 55) **2)** 30 years (SD ± 18.7) (range 2 to 72) **Gender Mix:** **1)** M/F = 5 (41.7%)/7 (58.3%) **2)** M/F = 10 (71.4%)/4 (28.6%) **Repeat Resections:** **1) & 2)** 0% **Inclusion Criteria:** Patients with supratentorial cavernomas in critical brain areas **Exclusion Criteria:** Not stated	All patients had complete resection of tumour. The IMRI patients did not require further resection after IMRI. No major morbidity or mortality occurred in either treatment group. 63.6% of IMRI patients who had preoperative seizures were seizure free after tumour resection, compared to 62.5% in the conventional group. 21.4% of IMRI patients exhibited postoperative clinical improvement, compared to 41.7% in the conventional group. No clinical deterioration was evident in the conventional group whereas 14.3% deteriorated in the IMRI group.	Retrospective study design. Treatment allocation was not random. Unclear what criteria were used to decide which patients underwent IMRI. Diverse patient group with a wide range of symptom severity. Prognostic factors, such as seizure history and lesion location, were not controlled for. The neuronavigation set up differed between groups since functional data was included for only some patients.

IMRI – interventional/intraoperative magnetic resonance imaging; SD – standard deviation

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Authors/ Location	Intervention	Study Design	Study Population	Results	Comments
Hall et al.[53,77] Minnesota, USA	**1) Conventional operative procedure** No details given. **2) IMRI procedure** A short bore 1.5 T magnetic resonance scanner (ACS-NT, Philips Medical Systems) was used for imaging. Images were obtained intermittently during planned interruptions in surgery by moving the patient to the magnet.	Retrospective non-randomised case matched controlled cost-effectiveness study **Case Matching Criteria:** Diagnosis codes related to neoplasms of the brain **Mean Follow-up:** **1)** Not stated **2)** *Age < 18 years:* 18.0 months; *Age ≥ 18 years:* 11.3 months; *Combined range:* 2.7 to 24.4 months **Setting:** University affiliated medical centre **Study Period:** **1)** 1993 to 1998 **2)** May 1997 to June 1999 **Outcome Measures:** Length of hospital stay; hospital direct and indirect costs, charges, and payments; readmission rates; repeat resection interval; and net health outcome	**Sample Size:** **1)** *Age < 18 years:* n = 12; *Age ≥ 18 years:* n = 35; **2)** *Age < 18 years:* n = 12; *Age ≥ 18 years:* n = 35 **Number of procedures:** **1)** Not stated **2)** *Age < 18 years:* n = 14; *Age ≥ 18 years:* n = 37 **Patient Diagnosis:** Craniotomy for tumour resection **Mean Age:** **1)** Not stated **2)** *Age < 18 years:* 11.1 years (range 1.2 to 17.8); *Age ≥ 18 years:* 46.3 years (range 20.6 to 73.4) **Gender Mix:** **1)** Not stated **2)** *Age < 18 years (n = 14 procedures):* M/F = 5 (35.7%)/9 (64.3%); *Age ≥ 18 years (n = 37 procedures):* M/F = 24 (64.9%)/13 (35.1%) **Repeat Resections:** **1)** Not stated **2)** Age < 18 years (n = 14 procedures): n = 8 (57.1%); Age ≥ 18 years (n = 37 procedures): n = 25 (67.6%) **Inclusion Criteria:** Patients undergoing craniotomy brain tumour resection **Exclusion Criteria:** Patients whose inpatient stays were coded with diagnosis codes that were not related to neoplasms of the brain.	Length of hospital stay was 54.9 % shorter for adult IMRI patients undergoing initial resection ($p < 0.0001$) and 31.0% shorter for repeat resection ($p < 0.05$), compared to the conventional procedure group. For pediatric patients, these values were 68.1% ($p < 0.0005$) and 39.8% (not statistically significant), respectively. Total hospital costs for adult IMRI patients undergoing first and repeat resection were lower by 14.1% (not statistically significant) and 3.3% (not statistically significant), respectively, in comparison to the conventional group. For pediatric patients these values were 46.4% ($p < 0.01$) and 44.7% ($p < 0.05$), respectively. No IMRI patients required subsequent neurosurgery in the follow-up period. The repeat resection rate for adults and children in the conventional group was 18.2% and 31.7%, respectively.	Retrospective study design. Treatment allocation was not random. Anesthetic and postoperative management was not stated for either group. Lesion matching was based on very limited criteria. Prognostic factors, such as seizure history and lesion location, were not controlled for. Did not address impact on morbidity or quality of life.

IMRI – interventional/intraoperative magnetic resonance imaging

APPENDIX B: SEARCH STRATEGY

Table B.1 lists the databases and information sources searched to identify literature and related materials. The bibliographies of all publications retrieved in full hard copy form were manually searched for relevant references that may have been missed in the database searches.

The Medical Subject Headings (MeSH) used were: "magnetic resonance imaging", "intraoperative period", "intraoperative care", and "operating room". Other keywords used were intra-operative, IMRI, MRI, magnetic. Variations of these keywords were used alone or in combination in the following electronic databases and websites.

Table B.1: Databases and search terms used in the search strategy

Database	Edition	Platform or URL	Search Terms†
Cochrane Library	Issue 4, 2003	Network license	(intraoperative next mri) OR (intraoperative next magnetic) OR (intra-operative next magnetic) OR (intra-operative next mri) OR "interventional MR imaging" OR (interventional AND Magnetic Resonance Imaging) OR iMRI
ECRI IHTA and Healthcare Standards Databases	Searched January 8, 2004	http://www.ecri.org/	(intraoperative OR intra-operative OR imri OR iMRI OR interventional) AND (MRI OR Magnetic Resonance Imaging OR MR imaging)
HealthSTAR	Searched December 18, 2003	OVID	(operating room OR intraoperative period OR intraoperative care OR "interventional MR imaging" OR interventional OR iMRI OR imri) AND (MRI OR magnetic resonance imaging OR MR Imaging)
EMBASE	Searched December 18, 2003	OVID	(Intraoperative Period/ OR intraoperative OR intra-operative) AND (Nuclear Magnetic Resonance Imaging OR MRI OR magnetic resonance imaging)
Web of Science	Searched December 18, 2003		(MRI OR magnetic resonance imag* OR MR imaging) AND (intraoperative OR intra-operative OR interventional OR iMRI OR imri)
PubMed	Searched December 18, 2003	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=icauahslib	(intra-operative OR intraoperative OR "intraoperative care" OR "intra-operative care" OR interventional OR imri OR IMRI) AND (MRI OR MR imaging OR Magnetic Resonance Imaging OR magnetic resonance)
Alberta Health and Wellness	Searched January 8, 2004	http://www.health.gov.ab.ca/coverage/index.html	MRI OR magnetic resonance OR MR imaging

Database	Edition	Platform or URL	Search Terms†
Alberta Medical Association Clinical Practice Guidelines Program	Searched January 8, 2004	http://www.albertadoctors.org/resources/guideline.html	MRI OR magnetic resonance OR MR imaging
Blue Cross Blue Shield	Searched January 8, 2004	http://www.bluecares.com/healthprofessionals/tec.html	MRI OR magnetic resonance OR MR imaging
Cabot	Searched January 8, 2004	http://www.mycabot.ca	MRI OR magnetic resonance OR MR imaging
Clinical Trials Database (US)	Searched December 18, 2003	http://www.clinicaltrials.gov/	(magnetic resonance OR MRI OR MR imaging) AND (intra* OR interventional)
CMA Clinical Practice Guidelines Database	Searched January 8, 2004	http://mdm.ca/cpgsnew/cpgs/index.asp	(intra-operative OR intraoperative OR interventional) AND (MRI OR Magnetic Resonance Imaging OR MR imaging)
Health Canada – Medical Device Licenses Issued	Searched January 8, 2004	http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/mdlic_e.html	intraoperative OR intra-operative OR interventional OR MRI OR MR OR magnetic resonance
Institute for Clinical Systems Improvement	Searched January 8, 2004	http://www.icsi.org/	MRI OR magnetic resonance OR MR imaging
National Research Register (UK)	Issue 4, 2003	http://www.update-software.com/nrr/CLIBINET.EXE?A=1&U=1001&P=10001	(magnetic resonance OR MRI OR MR imaging) AND (intra* OR interventional)
NICE	Searched January 8, 2004	http://www.nice.org.uk/	MRI OR magnetic resonance OR MR imaging
STEER	Searched January 8, 2004	http://www.wihrd.soton.ac.uk/projx/signpost/welcome.htm	MRI OR magnetic resonance
University HealthSystem Consortium	Searched January 8, 2004	http://www.uhc.org	Searched publication list
US Medicare Coverage Database	Searched January 8, 2004	http://www.cms.gov/coverage/	MRI OR magnetic resonance OR MR imaging

Database	Edition	Platform or URL	Search Terms†
FDA website and 510(k) Database	Searched January 8, 2004	http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm	(MRI OR magnetic resonance imag* OR MR imaging) AND (intraoperative OR intra-operative OR interventional)
CRD Databases (DARE, NHS EED, HTA Database)	Searched January 8, 2004	http://agatha.york.ac.uk/welcome.htm	intraoperative MRI OR intraoperative magnetic OR intra-operative mri OR intra-operative magnetic OR interventional MRI OR "interventional MR imaging" OR (interventional AND Magnetic Resonance Imaging) OR iMRI
NLM Gateway	Searched January 8, 2004	http://gateway.nlm.nih.gov/gw/Cmd	intraoperative MRI OR intraoperative magnetic OR intraoperative MR OR intra-operative mri OR intra-operative magnetic OR intra-operative MR OR interventional MRI OR interventional magnetic OR interventional MR
National Guideline Clearinghouse	Searched January 8, 2^04	www.guideline.gov	(intra-operative OR intraoperative OR interventional) AND (MRI OR Magnetic Resonance Imaging OR MR imaging)
AETMIS	Searched January 8, 2004	http://www.aetmis.gouv.qc.ca/en/index.php?menu=1	(intra-operative OR intraoperative OR interventional) AND (MRI OR Magnetic Resonance Imaging OR MR imaging)
CCOHTA	Searched January 8, 2004	http://www.ccohta.ca/publications/pubs_e.asp	(intra-operative OR intraoperative OR interventional) AND (MRI OR Magnetic Resonance Imaging OR MR imaging)
Copernic Metabrowser	Searched January 9, 2004		"intraoperative MRI" OR "intraoperative MR" OR "intraoperative magnetic" OR "intra-operative MRI" OR "intra-operative MR" OR "intra-operative magnetic" OR "interventional MRI" OR "interventional MR" OR "interventional magnetic"
Google	Searched January 9, 2004	http://www.google.com	"intraoperative MRI" OR "intraoperative MR" OR "intraoperative magnetic" OR "intra-operative MRI" OR "intra-operative MR" OR "intra-operative magnetic" OR "interventional MRI" OR "interventional MR" OR "interventional magnetic"

Note: * is a truncation character that retrieves all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc.
†Searches were limited to human and English language studies published from 1990 onwards.

APPENDIX C: METHODOLOGY

Inclusion and exclusion criteria

Types of Studies

Only prospective randomised controlled trials or non-randomised comparative studies, with at least ten patients in each study arm, published in English from 1990 onwards were included for analysis.

Index intervention

Any interventional or surgical procedure that utilised near real-time MR imaging to guide or monitor aspects of the procedure at the time that it was being performed.

Comparator intervention

The same intervention or procedure as the index intervention but performed without IMRI.

Participants

Data were collected on patients undergoing IMRI for any indication. Animal studies were not included.

Outcomes

The papers included must contain information on at least one of the following outcomes of the new or comparative intervention. In addition, at least one of these outcomes must be reported for both the index and the comparative intervention to allow for comparison between the treatment groups. These outcomes may include but not be limited to:

- Perioperative and postoperative mortality of patients;
- Postoperative morbidity of patients which may include hemorrhage, neurological deficit, and infection;
- Perioperative and postoperative efficacy measures which may include operative time, discomfort and/or pain, length of hospital stay, tumour recurrence rate, need for further treatment, and quality of life score.

Background Information

Where appropriate, relevant published material in the form of narrative reviews, letters, conference material, commentary, technical reports, editorials and abstracts were included as background information.

Expert review

In selecting reviewers, the AHFMR chooses experts who are well recognised and published in the peer-reviewed literature, and who can offer a provincial and/or national perspective with respect to the use or practice of the intervention under assessment.

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